Systems biology, big science and grand challenges

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Abstract
Systems biology is currently one of the most prominent large-scale endeavours in the life sciences, so it might be considered to be a good example of 'big science'. Further analysis shows, however, that although systems biology does make use of use of huge quantities of data, requires large amounts of funding, and is highly interdisciplinary and collaborative, in other respects it does not fit comfortably under the heading of big science. I suggest that we need to adopt new policy categories if we want to understand the dynamics of the contemporary life sciences. The term 'New Biology' has been used to identify recent changes. New Biology involves the integration of many different disciplines, and, importantly, it is oriented towards addressing major societal needs or 'grand challenges'. I ask: if 'big science' was the language of the twentieth century, are 'grand challenges' the language of the twenty first? I end by arguing for the increased involvement of the social sciences and humanities in the formulation of grand challenges.

Keywords: systems biology, big science, grand challenges, new biology, interdisciplinarity

Introduction

Systems biology attempts to integrate and make sense of the vast amounts of biological data that have been collected in recent years. The field is interdisciplinary and ambitious, so we might think it should uncontroversially be classified as 'big science'. But in the 36 interviews I carried out with systems biologists from Europe, the US and Japan, there was only one mention of the term 'big science'. This was in the context of a discussion about how systems biology will become *small* science, because of the down-sizing of experimental facilities due to higher precision experimental techniques such as microfluidics. What am I to make of this finding? Does it merely reflect the contingencies of the interview situation? Does it mean 'big science' is not an actors' category in this field? Does it mean systems biology is not big science?

I start this paper by introducing systems biology and discussing the extent to which it possesses those features that are commonly attributed to big science. This analysis was developed for the workshop that cumulated in this special edition, which was an exploration of the rise of 'big biology' (see Davies et al. this volume).[1] The exercise does reveal some key features of systems biology, particularly when contrasted to synthetic biology, but I go on to suggest that to understand the dynamics of the life sciences today we need to move beyond 'big science' – a policy category developed in a post-war funding environment and centred on physics (Smith 1992). 'New Biology' is a term which has recently been used to try to capture current changes. I critically analyse the New Biology discourse, and its application to systems biology, focusing particularly on a report published by the US National Research Council. One of the central features of New Biology is that it should be directed to certain pre-defined societal goals, or grand challenges. I argue this is a demonstration of a broader rhetorical shift away from 'big science' towards 'grand challenges', and that what lies behind these policy categories are ideas about what we value as a society. There is a hope that New Biology, oriented towards grand challenges, will make biology bigger, faster, but most importantly, better.

This paper discusses systems biology, and to a lesser extent synthetic biology, but since I consider them in the light of the policy categories 'big science', 'new biology' and 'grand challenges', this enables me to broaden my perspective on these subdisciplines. Such a broad perspective is necessary since we are arguably in the 'century of biology', and it is common to hear claims for the potential of biology which stretch far beyond its academic contributions. For example, Smolke and Silver (2011) argue that "Biology is the technology of this century. The potential uses of biology to improve the human condition and the future of the planet are myriad" (p.855). My aim is to analyse policy narratives about the power of biology to produce social progress, and the ways in which the life sciences are presented as the means to address grand challenges. I also reflect on the place of the social sciences in these discussions.

[1] 'Making it Big? Tracing collaboration, complexity and control in the biosciences' Exeter, 17-18 March 2011.

This paper draws on policy documents, empirical material, and scientific literature on systems biology. The empirical material includes the 36 interviews with systems biologists mentioned above and ethnographic work in the field (including attendance at systems biology conferences and workshops, and extended stays in three systems biology laboratories in the UK and the US), as well as ongoing research in synthetic biology. Although I do make use of this empirical data, my primary aim is to contribute to the analysis of the assumptions and implications of policy categories.

Systems biology as big science

Systems biology can be defined as "an integrative research strategy designed to tackle the complexity of biological systems and their behavior at all levels of organization (from molecules, cells and organs to organisms and ecosystems)" (Auffray et al. 2009:1). It emerged in the late 1990s, enabled by the availability of large amounts of biological data, particularly from the genome sequencing projects, as well as advances in computing power (Powell et al. 2007). Figures such as Leroy Hood and Hiroaki Kitano were influential in establishing the field in the US and Japan respectively. At first glance, systems biology seems to be an excellent example of big science. Caplan (2010), for example, says "Systems Biology tends to be seen as belonging to the world of programmatic, multi-lab, very expensive "big science"" (p.58).

As Caplan implicates, considerable amounts of funding have been directed to systems biology in recent years. Macilwain (2011) calculates that approximately $330 million is spent on systems biology per year in the US, $30-50 million in Japan, €50 million in Germany, and that the UK spent £73 million on systems biology from 2005-12. Aside from funding, there are other indications of the growth of systems biology, such as an annual meeting attracting 1200 attendees in 2010, and a growing number of publications, rising from "a handful" in 2001 to nearly 2000 in 2009 (Chuang et al. 2010). In the last ten years there has been a rise in the numbers of chairs, departments, institutes, and journals dedicated to systems biology (Powell et al., 2007). This does not mean systems biology has become mainstream, however. Macilwain (2011) points out that "a large and increasing number of cell biologists, immunologists, and other biologists are incorporating systems approaches into their work, but the cadre of researchers expressly devoted to systems biology remains relatively small" (p.840).

When asked to define systems biology, scientists working in the field will often say that it is an 'approach', with the broad goal of increasing biological understanding (Calvert and Fujimura 2011). The proponents of systems biology say it should be compared to molecular biology, because like molecular biology it is a 'paradigm shift' (their words) in the way in which we make sense of biological systems. These features do not fit well with some of the features commonly attributed to 'big science', which is often defined as a "large-scale project" (Bartlett 2008:51) with a defined goal. A classic example of such a project would be the Manhattan Project, and a biological example is the Human Genome Project. Although there are undoubtedly project-like activities which go on *within* systems biology, such as the silicon cell[2] or the virtual liver[3], systems biology is broader than these projects.

The comparison to molecular biology is helpful here. It might be considered rather strange to describe molecular biology as ‘big science’, because it is a foundational approach to the study of biological systems. Proponents of systems biology hope that it, like molecular biology, will become subsumed into the rest of biology, and will become part of everyday biological research. For example, the UK’s Biotechnological and Biological Sciences Research Council (BBSRC 2011) says it will “make systems approaches more ‘routine’ in bioscience” (p.9), and that this will enable a deeper understanding of complex biological systems.

One way in which systems biology is undoubtedly big, however, is in terms of “the mountains of new data” (Chuang et al. 2010:23.4) it aspires to make sense of. The computational tools and mathematical models used by systems biologists have made it possible to work with previously unprecedented levels of molecular data, and have allowed the integration of many different types of data. Some systems biologists argue that their work is not qualitatively different from the molecular biology that preceded it, but that it is quantitatively different because it draws on larger amounts of data. One of my interviewees had a revealing quotation from the philosopher A. N. Whitehead attached to his office door: “It is not the imagination of man that improves but his capacity to measure which increases”. Others interpret the situation less positively, describing systems biology as “the name of the crisis; it’s the name of the fright that everyone’s gone into about having all the pieces and still not knowing how biology works” (Interview34).

Systems biology attempts to understand biological systems by bringing in quantitative expertise from disciplines such as physics, engineering, mathematics and computer science (McCarthy 2004). This makes systems biology extremely interdisciplinary and collaborative and, in this sense, ‘big’. Since it brings together diverse disciplines with different ideas about appropriate methodology and about what constitutes ‘good science’, systems biology is currently best understood as a constellation of different ‘epistemic cultures’ (Knorr-Cetina 1999), rather than a unified approach (Kastenhofer 2013). Attempts to coordinate the activities of these different groups have made interdisciplinary collaboration, and the attendant difficulties of facilitating communication and bringing people together under the same roof (which is often the aspiration, despite the *in silico* nature of much of the work), some of the most important challenges facing systems biology.

Despite these challenges, systems biology is an excellent example of a field that is explicitly interdisciplinary, if this is defined as the integration and synthesis of perspectives from different disciplines (see Barry et al. 2008; Thompson Klein 1990). This interdisciplinarity is driven both by the object of study and the questions that are being asked. As I argue elsewhere (Calvert 2010), systems

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[2] http://www.siliconcell.net/
[3] http://www.virtual-liver.de/

biology is presently best understood as an emergent phenomenon resulting from the coordination of multiple sets of expertise, although some hope in the future both 'wet' and 'dry' skills could reside within one 'moist' individual, and that we will see a movement from specialists to 'integrators' (Interview1).

This interviewee's use of the word 'integrators' is telling, because integration is a term that is often heard in systems biology. It is sometimes used to refer to data integration (systems biology centres often have posts specifically dedicated to data integration), but the term can be used in a more conceptual sense. For example, Denis Noble (2006), a leading UK systems biologist, says systems biology "requires a quite different mind-set. It is about putting together rather than taking apart, integration rather than reduction…this is a major change. It has implications beyond the purely scientific" (p.xi). Some scientists prefer the term 'integrative biology' to 'systems biology' (Interview17) and others talk of integration across various scales in systems biology, from the molecular to the cellular to the organismal (Butcher 2004). Integration is even drawn upon as a defining feature of systems biology. One senior scientist says: "you would probably say 'well we have been studying systems for years'. In an integrated way, absolutely not" (Interview20).

Integration is considered to be necessary to tackle the complexity of biological systems, and "understanding complexity" (Interview 18) is identified by some as the central focus of systems biology. It could even be argued that the 'bigness' of systems biology (in terms of the extent of its interdisciplinary collaborations) is simply a demonstration of the organisational arrangements that are necessary to systematically analyse biological complexity.

In its attempts to make sense of complexity, systems biology can be understood as a successor to the Human Genome Project – the exemplar of big science in a biological context. Genomics is often portrayed as a disappointment by systems biologists, and many of my interviewees talked about how it failed to deliver, both in a socio-economic sense of providing cures for diseases, and in a conceptual sense of providing an understanding of the complexity of organismal function. Arguments are made that systems biology has moved beyond genomics because it has confronted the fact that knowing components is not the same as knowing life (Interview33). This ties into discussions of emergence, which can be roughly defined as the idea that the whole is more than the sum of its parts, and that context and interactions must be taken into account (Powell and Dupré 2009). The context provided by the cell, the organism, and its environment (both natural and social) becomes relevant to the study of biological systems.

Another way in which systems biology differs from the Human Genome Project is that the latter was considered to raise many ethical, legal and social issues (ELSIs), to such an extent that 3-5% of the total funding was allocated to work under the ELSI heading (DoE 2011). If an ELSI component is a necessary feature of big biology then it is notable that systems biology has not received much attention in this respect, despite promising extremely beneficial outcomes for science and society (ESF 2005). O'Malley et al. (2007) argue this lack of attention is due to the somewhat elusive nature of the object of study in systems biology. It is harder to attach social and ethical issues to an object that is interactive and dynamic (a biological system) than to one that is static (a gene).

A significant contrast here is with synthetic biology, which has received a great deal of attention from social scientists, lawyers and bioethicists, even though systems biology is more established and has been better funded.[4] In fact, in many countries ELSI involvement is a requirement for getting funding in synthetic biology, but not in systems biology. Since I study both of these fields I find this difference intriguing.

Synthetic biology, like systems biology, can be understood as a reaction to biological complexity, but rather than embracing this complexity as systems biology does, synthetic biology attempts to manage it by creating novel standardized biological parts and devices (Endy 2005). Its proponents argue that these parts and devices will be used to produce useful drugs and chemicals, green fuels and tools for bioremediation (RAE 2009). The possible (accidental or intentional) release of novel organisms into the environment attracts the attention of policy makers and regulators.

This raises interesting questions about when an area of biological research becomes a matter of policy and regulatory concern. I have often been surprised at the willingness with which policy makers will engage with the 'issues' raised by synthetic biology, while systems biology is left on the sidelines. Synthetic biology seems to fit into discourses of 'risk' and 'harm' that are the subject of many existing policy debates. Previous work on genetically modified crops or nanotechnology can easily be adapted to synthetic biology, sometimes by simply deleting the word 'nanotechnology' and inserting 'synthetic biology'. If it is the case that there is a coherent class of activities called 'emerging technologies', which share a lack of fit with existing institutions and the potential to disrupt regulatory regimes, this is of course a totally legitimate practice. And it could be argued that synthetic biology is an emerging technology like nanotechnology, while systems biology has more in common with foundational approaches to the study of biological systems like molecular biology, as argued above. But does the carrying over of issues from areas such as nanotechnology into synthetic biology imply a narrow and predetermined framing of what is important in this field? And should social scientists necessarily pay more attention to the topics that receive more attention from policy makers?

In recent years 'ELSI' programmes have become associated with many new areas of the life sciences, such as stem cell research and neuroscience as well as synthetic biology (Calvert and Martin 2009). Webster (2007) has observed that in emerging technologies like these new relations between science, technology and society are being created, which provide new spaces for intervention. However, social scientists, ethicists and lawyers have not been drafted in as 'ELSI' add-ons to systems biology in the same way. It is not that they have been excluded – in fact, funders have been positive about social scientific interest in

[4] Zhang et al. (2011) list 39 reports published since 2004 on synthetic biology and its implications.

systems biology from its early stages, and systems biologists are themselves often very interested in interacting with scholars from the social sciences and humanities. The interdisciplinary collaborations required by systems biology mean the value of a sociological perspective on the field is clear to most of its practitioners, and the epistemic differences between collaborating disciplines concerning what constitutes 'good' scientific method leads some systems biologists to pursue joint work with philosophers of science (for example O'Malley and Soyer 2012). But unlike their colleges in synthetic biology, they are not *required* to collaborate. This means that in systems biology the social scientist is often in the traditional role of the observer, reflecting on the science, but not implicated and involved in the production of knowledge. This is in contrast to synthetic biology, where difficult issues arise about the obligations, responsibilities and challenges of being an 'entangled' social scientist in the field.[5]

Although systems biology has not captured the public imagination in the same way that synthetic biology has, there are some 'issues' that do give rise to discussion in systems biology. These include: *in silico* prediction of disease, the patenting of networks of interacting molecules (Calvert 2008), and personalised medicine (Hood et al. 2004). A more subtle point, referred to in passing above, is the understanding that "life arises not from the isolated molecules but in their communication" (Westerhoff 2005). Although it is rarely discussed, systems biology could encourage us to understand life as a network of relations that is emergent, dynamic and interconnected, and this could have implications for public understanding, regulation and policy.

Despite the apparent lack of attention to the 'issues' that are 'raised' by systems biology (an extremely problematic framing), systems biologists regularly stress the importance of involving disciplines from outside the natural sciences and engineering in their work. This breadth of interdisciplinary ambition is perhaps the most striking feature of the field. Some maintain that systems biology has 'no walls', but it just draws on expertise from whichever areas are most useful or appropriate at the time (Interview8). One biologist even said he wanted to "to eliminate the barriers between disciplines and say 'science is science'" (Interview32). In such a context where the differences between disciplines could become less important, we might be inclined to adopt an understanding of science more aligned with the German *Wissenschaft*, which incorporates the social sciences and the humanities. In this light, we should perhaps reinterpret 'big science' in a more literal manner. Systems biology might be big science in the sense that it extends our understanding of what we should think of as 'science'.

This notion of big science takes us far from the realm of science policy, and it is helpful to ground this discussion of systems biology by recognising that if something is labelled 'big science' then a policy decision has been made that a particular area of research is deserving of funding. This means that a discussion of big science is importantly a discussion of research priorities (Hevley 1992). The setting of research priorities is a crucial issue in science policy, because it

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[5] I am exploring these issues in other work (see Calvert forthcoming).

has epistemic as well as practical consequences since it has an important influence on what research is undertaken and what comes to be known. There are questions to be asked about why governments across the world have decided that systems biology is a valuable area to fund, in the face of competing pressures and budgetary demands. These questions will be addressed in the discussion of New Biology below.

Understanding the dynamics of the life sciences

The previous section has shown that thinking of systems biology in terms of big science is revealing in some respects. Systems biology is not a discrete project, but it does require large amounts of funding, it makes use of huge quantities of data, and it is highly interdisciplinary and collaborative. However, it seems that we are coming up against the limits of big science as an analytical tool if we want to answer broader questions about the changes that are occurring in the life sciences, and how we should make sense of them.

The term 'New Biology' has been used in several contexts to try to engage with these dynamics. It aims to encapsulate the idea that biology is changing rapidly and substantially and that this extends beyond the analysis of new subfields such as systems or synthetic biology. The most prominent discussion of this topic is the US National Research Council's (NRC's) 2009 report *A New Biology for the 21st Century*.[6] This was written by a panel of 16 leading biologists "to determine how biology could best capitalize on the wellspring of technical advancements inundating the field" (Macilwain 2011:839). This report is, of course, not the only recent report addressing current trends in the life science, but I focus on it here because it is representative of topics that are being more widely discussed, it is influential, and it discusses both systems and synthetic biology.

The report starts by claiming that "Biological research is in the midst of a revolutionary change due to the integration of powerful technologies along with new concepts and methods derived from inclusion of physical sciences, mathematics, computational sciences, and engineering" (p.vii). What makes 'New Biology' new is that disciplines are coming together than would not do so normally.[7] The report goes on to emphasise the importance of integration, a key notion in systems biology as has been discussed above. It says "the essence of the New Biology is integration – re-integration of the many subdisciplines of biology, and the integration into biology of physicists, chemists, computer scientists, engineers, and mathematicians to create a research community with the capacity to tackle a broad range of scientific and societal problems" (p.vii). But what is notable about the report is its almost complete exclusion of the social sciences, law and the humanities. There is only one brief mention of social science in the whole report, when it is admitted that "Science and technology alone, of course,

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[6] The title of the report is similar to Woese's (2004) well known paper 'A new biology for a new century', and Woese's ideas are cited in the NRC report.

[7] We should, of course, be sceptical of anything that claims to be 'new'. Molecular biology similarly brought together biologists, physicists, chemists and mathematicians to address biological questions in the 1940s-50s, and the beginning of the 20th century saw the rise of 'general biology', which aspired to combine many different strands of research (Powell et al. 2007).

cannot solve all of our food, energy, environmental, and health problems" and that "Political, social, economic, and many other factors have major roles to play in both setting and meeting goals in these areas" (p.10).

The report focuses on recent scientific advances that have allowed biologists to "integrate biological research findings, collect and interpret vastly increased amounts of data, and predict the behavior of complex biological systems" (p.1). This is an excellent description of systems biology, but systems biology is not explicitly mentioned in the report until page 49. Here there is a brief discussion of the three 'foundational sciences' needed for the rise of the New Biology, namely systems biology, computational biology and, interestingly, synthetic biology (which is usually thought of as an application-driven field, rather than a 'foundational science'). The discussion of systems biology emphasises the importance of predictive models and "deep quantitative understanding of complex biological processes" (p.62).

Systems biologists have not been slow to recognise the report's relevance to their endeavours. For example, Leroy Hood, the founder of the Institute for Systems Biology (ISB), has written: "Imagine our delight when the National Academy of Sciences recently released a report that articulated the nature of an emerging "new biology" that described perfectly the systems biology of ISB" (Hood 2009:1), later implying the terms could be used interchangeably by using phrase: "systems biology (or the "new biology")" (p.1).

Although the New Biology report is US focused, we see similar ideas in other national contexts. For example, the BBSRC (2011) wants to ensure "that the UK stays internationally competitive by driving data intensive and multidisciplinary approaches to bioscience to deliver new, deeper understanding of how complex living systems function" (p.3). As this reference to international competitiveness indicates, these arguments for the importance of the interdisciplinary life sciences are closely tied to broader political agendas. And one of the most notable features of the New Biology report is that it sees biology as being oriented towards important societal challenges. For example, it claims that "As never before, advances in biological sciences hold tremendous promise for surmounting many of the major challenges confronting the United States and the world" (p.vii). This emphasis on 'grand challenges' is significant, because I want to suggest that while 'big science' was the language of the twentieth century, 'grand challenges' is the language of the twenty first. 'Grand', after all, is a kind of synonym for 'big'. Like big science, grand challenges are ways of signalling research priorities.

Grand challenges

According to Brooks et al. (2009) the essence of the grand challenge idea is that "bringing together optimal combinations of human minds and scientific institutions around a specific problem or goal is the surest route to finding solutions to the world's biggest problems" (p.8). Grand challenges galvanise research efforts, and they can be addressed from a range of different perspectives. They are necessarily interdisciplinary challenges, and the type of interdisciplinarity we see here is one that is motivated by the problem being addressed.

The use of 'grand challenges' in today's policy discussions is highly influenced by the Gates Foundation's 'Grand Challenges in Global Health', a programme launched in 2003 in collaboration with the US National Institutes of Health to improve the health of the poorest people in the world (Omenn 2006). Although this is perhaps the most prominent of the grand challenge initiatives, retrospective (and perhaps anachronous) discussions of 'grand challenges' sometimes trace them back as far as 1714 when the British Parliament offered a prize for the Calculation of Longitude. A more commonly cited origin for the idea of grand challenges is 1900 when the mathematician David Hilbert produced a list of 23 important unsolved mathematics problems (Brooks et al. 2009). However, although Hilbert used the language of 'grand challenges', these challenges were internal to mathematics, so they are not being used in the mission-oriented sense that we see in the more recent policy discourse.

Other historical examples of grand challenges that are given include a chess playing computer in the 1950s, President Kennedy's commitment to "landing a man on the moon and returning him safely to Earth" in the 1960s,[8] and Nixon's War on Cancer in the 1970s (Omenn 2006). But it was in the 2000s, following the Gates Foundation initiative, that grand challenges became "a tool for mobilising an international community of scientists towards predefined global goals with socio-political as well as technical dimensions" (Brooks et al. 2009:9). Notably in 2009 the Lund Declaration, handed to the Presidency of the European Union by 400 prominent researchers and politicians, stated unambiguously that "European research must focus on the Grand Challenges of our time moving beyond current rigid thematic approaches" (Lund Declaration 2009:1).

Today there are grand challenges in many sectors. For example, the US National Academy of Engineering has a list of grand challenges which includes making solar energy more economical, providing universal access to clean water, and reverse engineering the brain.[9] The BBSRC has three grand challenges: food security, sustainable bioenergy and enhancing lives and improving wellbeing. There is something about the urgency and ambition of grand challenges which makes them appealing, and it is common for researchers in synthetic biology in particular to explicitly link their research to a key 'grand challenge' in their conference presentations.

One of the reasons why grand challenges are so interesting is because they contain assumptions about what we value as a society. They are clearly future oriented, but they orient us towards certain futures and away from others. This takes us back to the point made earlier about the importance of research priorities in science policy. As Jones (2010) puts it, grand challenges lead to questions that are "fundamentally questions of politics in its proper sense. They

[8] http://nasawatch.com/archives/2011/05/one-of-the-most.html
[9] http://www.engineeringchallenges.org

are questions about what sort of world we want to live in and what kinds of lives we want to lead".

Grand challenges are often top down, and chosen by a government organisation or non-profit body. But sometimes a broader range of viewpoints is included. For example, the BBSRC (2011) says they consulted business, academic, and policy stakeholders when devising their grand challenges. Views of the public have been incorporated in some cases, such as in the UK nanoscience grand challenges. Kearnes (2009) interprets these moves as demonstrating "the increasing invocation of "the social" in contemporary innovation governance" (p.17). Grand challenges potentially allow for a more expansive social debate about funding priorities, but because they are often formulated 'from above', opportunities to contribute to their framing can be limited. A related concern is that grand challenges have to be constructed in terms of problems that science and technology can solve. Brooks et al. (2009) argue that they lend themselves to technical solutions, and this "trumps consideration of alternative possible trajectories – perhaps slower, or options for integrating technologies with social processes in different ways" (p.7).

Another potentially problematic feature of grand challenges is a consequence of their broad reach. They are 'grand' because they attempt to be global challenges, but Hulme (2010) has argued that this attempt to provide a "view from everywhere" is necessarily "insensitive to the peculiarities of place and context" (p.559), and is likely to impose culturally specific ideas about what is considered important. There is a danger that research priorities framed in terms of grand challenges could shut down other potentially productive avenues.

Because of their rising popularity grand challenges now cover an extremely diverse range of activities. Some grand challenges have clear societal relevance, while others are very difficult to distinguish from rather general scientific research questions. For example, two of the grand challenges that were introduced into the HGP in 2003 are: "Comprehensively identify the structural and functional components encoded in the human genome" (p.837) and "Elucidate the organization of genetic networks and protein pathways and establish how they contribute to cellular and organismal phenotypes" (Collins et al. 2003:838). These are scientific challenges, which are very different from the socially-oriented type of grand challenge put forward by the Gates Foundation.

This diversity of grand challenges is not necessarily problematic, however, because arguably one of the strengths of grand challenges is that they allow many different kinds of research to fit under a broad heading. Wienroth and Kearnes (2010) argue that there is room for researcher autonomy under the umbrella of societal challenge-led considerations. And the BBSRC (2011) says "Fundamental bioscience is *essential*" (p.5, emphasis in original) to find solutions to its grand challenges. This means there is an important place for systems biology in the grand challenge framework. Despite their problem-orientation, the ambition and the long time-scale of grand challenges have similarities with 'basic research', according to some definitions of this term (Calvert 2006).

A tentative suggestion in the light of these reflections is that with the introduction of grand challenges we might be witnessing a political renegotiation of the value of science. Although we do see a familiar agenda of national economic competitiveness and technological leadership in the discussion of grand challenges (in, for example, BBSRC 2011), many grand challenges are global, rather than national, and the issue of sustainability is often incorporated. The rhetoric seems to have shifted from that which dominated science policy in the 1980s and 1990s. Guston and Keniston (1994) and Elzinga and Jamison (1995) argue that during this period we saw the rise of the new contract away from researcher autonomy and toward closer links between academia and industry. But grand challenges take a step beyond this, toward broader social goals. The publicly stated priorities that are central to grand challenges could be seen as part of an attempt to establish a new contract for the public funding of science. This suggestion is supported by the Lund Declaration (2009), which identifies grand challenges as the third major policy rationale for funding science besides economic growth and competitiveness, and the Nuffield Council on Bioethics (2012), which argues that grand challenges "can act to leaven the relentless influence on economic drivers that dominates research policy" (p.104).

Although we do see resonances with previous discussions of changes in the research system where science is oriented towards strategic objectives – such as 'mode 2' (Gibbons et al. 1994), and 'post-normal science' (Funtowicz and Ravetz 1993) – the strength of grand challenges is their broadness and their vagueness, which allows them to encompass a greater diversity of research activities. As work on other categorisations has shown, vagueness and imprecision can in fact make such research categories more useful as policy tools (Bowker and Star 1999).

Grand challenges and New Biology

The New Biology report is completely consistent with the grand challenge philosophy (although it prefers the language of 'societal challenges'). The report contends that the New Biology will address four pressing societal challenges: sustainable food production, protection of the environment, renewable energy, and improvement in human health. We are told that these four areas of societal need were chosen by the committee who authored the report, who expected that "both the scientific community and the public would find such goals inspirational" (NRC:66). This is clearly an example of the top-down selection of grand challenges.

The report draws parallels to previous initiatives that it argues had a similar character to its four societal challenges. The moon landing is referred to on many occasions, as is the sequencing of the human genome. Both are seen as ambitious projects which were initiated before the necessary scientific understanding and technological developments were in place. The lesson drawn from these examples is that "In each case, establishing a bold and specific target created unforeseen routes to solutions" (p.65). The report develops similar 'bold and specific' targets which it hopes will lead to equally important scientific and technological developments. However, we do see a recognition of the difficultly of defining grand challenges for areas or 'approaches' like systems biology. It is noted that while the HGP had a clear and definable endpoint "a similar endpoint for some of these interdisciplinary and cross-cutting projects may be more difficult to define" (NRC:73).

It is interesting that the War on Cancer is not mentioned at any point in the New Biology report, even though this may be a more appropriate parallel than the moon landing because it had to confront the unpredictability of biological systems. But it is perhaps telling that the importance of learning to predict the behaviour of biological systems (a key aim of systems biology) is an epistemic value which is emphasised throughout. There is the assumption that predictability is necessary to address the four societal challenges that are the focus of the report. A rather linear diagram of research is found on page 18, where "scientific integration" leads with an arrow to "deeper understanding of biological systems" which then leads (optimistically) to "Biology-based solutions to societal problems".

This diagram does include arrows to represent feedback between the different stages of innovation, but its overall linearity suggests that the link between biological research and societal challenges it is supposed to be addressing has not been thoroughly thought through. This raises broader questions about the status of policy documents such as the NRC report, which are clearly part of a political process, designed to secure funding for fields such as systems and synthetic biology, rather than to accurately describe the current state of the life sciences. Some might be tempted to see grand challenge talk as primarily rhetorical, since it is easy to connect most research that is already being funded to one grand challenge or another without overt steering or governance. But even if its power is mainly rhetorical, we should not overlook the influence of this type of policy language, which not only attracts the attention of politicians and publics, but also demands that scientists change the way they position their research and present their activities.

Conclusions

I started this paper showing how big science explains some of the features of systems biology but not others. This led me to look for other ways of trying to grasp the dynamics of the contemporary life sciences. I have suggested that the policy categories of 'New Biology' and 'grand challenges' can help us understand current changes. Grand challenges are adequately vague to encompass a broader range of research activities, but they are appealing in their orientation towards broader social goals. Whether we or not are seeing the rise of 'New Biology' (or perhaps 'Grand Biology') is a question that requires further analysis, but I hope to have made a start here.

I want to end by going back to two key issues: the importance of values in science policy and role of the social scientists in the interdisciplinary life sciences. I have argued that both 'big science' and 'grand challenges' are best understood as forms of research prioritisation (or at least the public presentation of research prioritisation), and any analysis of current changes in the life sciences should not ignore this larger funding context. There are undoubtedly epistemic reasons for the emergence of big science in biology, but these are inseparable from the political motivations. Importantly, questions of research prioritisation in science policy are questions about values. Values motivate the idea that orienting biology towards grand challenges will somehow make it better.

Grand challenges are interdisciplinary challenges, and what we see highlighted above all else in the New Biology report is a move towards greater interdisciplinarity in the life sciences. But I would argue for a broader and more ambitious conception of interdisciplinarity than we find in this report; one that extends to include the social sciences and humanities. This is because grand challenges show that we cannot separate scientific projects from social systems, but that they depend on each other. As we saw above, the incorporation of the social sciences into synthetic biology is already underway, and there is enthusiasm among the systems biology community to engage with a broader range of disciplines. I think that social scientists should embrace these opportunities, because they are well placed to play a more active role in formulating grand challenges in the life sciences, and critiquing them. There is interesting and important work to be done in drawing attention to which futures grand challenges enable and which they neglect, and in asking questions about what constitutes 'better' biology, and who gets to decide.

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